

E1

- 2) assaying the operation activity of said substance on said receptor and
- 3) comparing the operation activity of the aberrant receptor in (2) with the operation activity of the aberrant receptor without the substance, wherein a change in the operation activity of the aberrant receptor indicates that the substance causes the aberrant receptor to operate in a manner similar to the non-aberrant receptor.

E2 Jul 32

16. (three times amended) A method of screening substances for a substance for treatment of a disease in a mammal caused by an aberrant receptor, which has substantially changed affinity for substances that have a natural affinity for a non-aberrant receptor, comprising:

- 1) bringing the aberrant receptor into contact with a substance,
- 2) assaying the operation activity of said substance on said receptor,
- 3) comparing the operation activity of the aberrant receptor in (2) with the operation activity of the aberrant receptor without the substance, and
- 4) selecting a substance that causes the aberrant receptor to operate in a manner similar to the non-aberrant receptor, wherein the substance can be used to treat a disease caused by the aberrant receptor.

E3 Jul 33

17. (twice amended) A method of screening for a drug for restoring normal function to a signal transduction system of a cell having an aberrant receptor of a mammal suffering from a disease caused by the aberrant receptor which affects the signal transduction system of the cell, which comprises:

- 1) bringing the aberrant receptor into contact with a subject substance,
- 2) assaying the activity of said substance on said receptor,
- 3) comparing the operation activity of the aberrant receptor in (2) with the operation activity of the aberrant receptor without the substance, and
- 4) selecting a substance that causes the aberrant receptor to operate in a manner similar to the non-aberrant receptor, wherein the activity is an activity that restores the normal function of the cell.

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19. (twice amended) The screening method according to claim 16, wherein the aberrant receptor is encoded by a gene in the mammal, the method further

E4 Sub 31
comprising the step of selecting the receptor by comparing the gene encoding the aberrant receptor, isolated from a cell of the mammal, with a gene encoding the non-aberrant receptor, prepared from a cell of a mammal of the same species that does not carry the aberrant receptor.

E5 Sub 34
21. (twice amended) A method of preparing a substance for treatment of a disease in a mammal caused by an aberrant receptor having a substantially changed affinity for substances, which results in the substantial reduction in activity of the signal transduction system of cells having the aberrant receptor, the method comprising:

bringing the aberrant receptor into contact with a subject substance,
assaying the activity of said substance on the aberrant receptor,
selecting a substance that substantially operates the signal transduction system of the cell having the aberrant receptor wherein said activity is activity that restores wide-type activity of the receptor
and admixing the selected substance with a pharmaceutically acceptable carrier.

E6 Sub 32
22. (three times amended) The method according to claim 21, wherein the aberrant receptor, which has substantially changed affinity for substances, is encoded by a gene in the mammal and is isolated from a cell which expresses the gene encoding the aberrant receptor.

23. (three times amended) The method according to claim 22, wherein the gene encoding the aberrant receptor is selected by comparing the gene encoding the aberrant receptor, prepared from a cell of the mammal, with a gene encoding the non-aberrant receptor, prepared from a cell of a mammal of the same species that does not carry the aberrant receptor.

Sub 35
24. (three times amended) A method of screening for a substance capable of causing an aberrant receptor, which has substantially changed affinity for substances, to operate in a manner similar to a non-aberrant receptor comprising:
(1) expressing in a cell the gene encoding the aberrant receptor,

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- (2) isolating the aberrant receptor from the cell,
(3) providing a substance to the aberrant receptor,
(4) determining the operation activity of the substance on the receptor, and
(5) comparing the operation activity of the aberrant receptor in (4) with the operation activity of the non-aberrant receptor,
wherein a similar operation activity in (4) to the operation activity of the non-aberrant receptor indicates that the substance causes the aberrant receptor to operate in a manner similar to the non-aberrant receptor.

Please add the following new claims:

Sub 35 cont
-- 27. A method of screening for a substance capable of causing an aberrant receptor, which has substantially changed affinity for substances, to operate in a manner similar to a non-aberrant receptor comprising:

- (1) providing cells expressing the gene encoding the aberrant receptor,
(2) providing the substance to be screened to the cells expressing the aberrant receptor,
(3) determining the operation activity of said substance on said receptor, and
(4) comparing the operation activity of the aberrant receptor with the operation activity of the non-aberrant receptor, wherein a change in the operation activity of the aberrant receptor indicates that the substance causes the aberrant receptor to operate.

Sub 36
28. The method according to claim 14, wherein the operation activity is a change in intracellular concentrations of responding substances selected from the group consisting of cAMP, inositol phosphate and calcium ion.

29. The method according to claim 16, wherein the operation activity is a change in intracellular concentrations of responding substances selected from the group consisting of cAMP, inositol phosphate and calcium ion.

30. The method according to claim 17, wherein the operation activity is a change in intracellular concentrations of responding substances selected from the group consisting of cAMP, inositol phosphate and calcium ion.

31. The method according to claim 18, wherein the operation activity is a change in intracellular concentrations of responding substances selected from the group consisting of cAMP, inositol phosphate and calcium ion.

32. The method according to claim 19, wherein the operation activity is a change in intracellular concentrations of responding substances selected from the group consisting of cAMP, inositol phosphate and calcium ion.

33. The method according to claim 24, wherein the operation activity is a change in intracellular concentrations of responding substances selected from the group consisting of cAMP, inositol phosphate and calcium ion.

34. The method according to claim 26, wherein the operation activity is a change in intracellular concentrations of responding substances selected from the group consisting of cAMP, inositol phosphate and calcium ion.

35. The method according to claim 27, wherein the operation activity is a change in intracellular concentrations of responding substances selected from the group consisting of cAMP, inositol phosphate and calcium ion.

36. The method according to claim 21, wherein the activity of the signal transduction system of cells is a change in intracellular concentrations of responding substances selected from the group consisting of cAMP, inositol phosphate and calcium ion.

37. The method according to claim 22, wherein the activity of the signal transduction system of cells is a change in intracellular concentrations of responding substances selected from the group consisting of cAMP, inositol phosphate and calcium ion.